REMARKS

A. Regarding the Amendments

Claims 1-19 were previously canceled. Claims 20-37 are pending. Claims 20, 33, and 35-37 have been amended to claim the subject matter of the invention with greater particularity and specificity. Amendments to claims merely clarify the language of claims and correct minor typographical errors mentioned by the Examiner.

Specifically, claim 20 now recites:

> "forming a complex comprising a target biomolecule and a sensitizer-linked substrate molecule capable of recognizing the target biomolecule."

This limitation is disclosed throughout the original specification. See, e.g., page 22, line 28 through page 23, line 4; page 49, lines 11-16; page 8, lines 9-10, page 20, lines 24-26, and FIG. 1.

Further, each of claims 20 and 37 now recites "irradiating the complex to cause a emission signal from the sensitizer." This limitation is also disclosed throughout the original specification. See, e.g., page 48, lines 23-24; page 2, lines 12-16

Also, claims 20 and 37 now require that determining of the presence of the complex is conducted for analytical purposes, such as "to detect the target biomolecule" (claim 20) and "to identify the agent of interest" (claim 37). These limitations are also disclosed throughout the original specification. See, e.g., page 49, lines 22-30; page 7, line 24 through page 8, line 3.

Accordingly, it is respectfully submitted that no new matter has been introduced by the amendments.

With regard to allegedly defective declaration required by the Examiner in item 1 on page 2 of the Office Action, the Applicants respectfully point out that such requirement was made by the PTO previously and the new declaration was filed on May 2, 2002. The PTO issued Notice of Acceptance on July 11, 2002, by which it informed the Applicants that all the items in the application were acceptable.

B. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 20-37 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention (item 4 on page 2 of the Office Action).

Each of claim 20 and claim 37 has been amended to include the limitation "irradiating the complex to cause a signal emission by the sensitizer." It is submitted that this limitation provides the missing step mentioned by the Examiner. The Applicants disagree with the allegation that this step is "essential," and added the limitation solely in order to facilitate and expedite the prosecution of the instant application. Claims 33, 35, and 36 have been amended as suggested by the Examiner. The Examiner's suggestions regarding amending these claims are gratefully acknowledged.

Accordingly, it is submitted that the 35 U.S.C. § 112, second paragraph, rejection does not apply. Reconsideration and withdrawal of the rejection are respectfully requested.

C. Rejections Under 35 U.S.C. § 102 (a)

Claims 20-29, 31-34, and 37 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Wilker et al. (Agnew. Chem. Int. Ed. 1999) (item 10, page 3 of the Office Action). This rejection is respectfully traversed.

It is axiomatic that a valid rejection of a claim for anticipation by a reference requires that the reference explicitly or inherently describe all of the elements,

limitations, and relationships recited in the claim. It is submitted that Wilker et al. do not describe all the elements and limitations recited in each of claims 20 and 37, as amended. Specifically, claim 20 recites a method including "irradiating the complex to cause an emission signal from the sensitizer" in order "to detect the target biomolecule." Claim 37 recites a method including "irradiating the complex to cause an emission signal from by the sensitizer" in order "to identify the agent of interest" which "modulates the target biomolecule."

Wilker et al. fail to disclose a method for detecting either a target biomolecule or the modulating agent of interest. Wilker et al. only disclose substrates for delivery electrons and holes to active sites in proteins where it is difficult to access the active sites (referred to as "buried" active sites). Thus, the complexes proposed in Wilker et al. are designed for rapid oxidation/reduction of the protein, and are useful for studies of the role of the protein in the catalytic cycle. Wilker et al. are silent with regard to the spectroscopic methods for detection of target biomolecules or the modulating agents recited in claims 20 and 37.

Therefore, the Wilker et al. article fails to disclose every element of claims and, accordingly, is not a proper prior art reference under 35 U.S.C. § 102(a). Accordingly, each of claims 20 and 37 is patentably distinguishable over Wilker et al. Each of claims 21-29, and 31-34 directly or indirectly depends on claim 20 and is considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

In addition, claims 20-29, 31-34, and 37 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Wilker et al., Book of Abstracts, 1998 (Wilker '98) (item 11, page 4 of the Office Action). This rejection is respectfully traversed.

Claims 20 and 37 recite the methods described above. Wilker '98 only discloses sensitizer-linked substrates for rapid delivery of electrons and holes to buried active sites in proteins. One sensitizer that can be used, according to Wilker '98, is $[Ru(bpy)_3]^{2+}$.

Wilker '98 also describes a method for oxidation and reduction of heme of $P450_{cam}$ protein by using Ru(III) and Ru(I) derivatives. Wilker '98 fails to disclose methods for detection of target biomolecules or the modulating agents recited in claims 20 and 37.

Therefore, Wilker '98 fails to disclose every element of claims and, accordingly, is not a proper prior art reference under 35 U.S.C. § 102(a). Accordingly, each of claims 20 and 37 is patentably distinguishable over Wilker '98. Each of claims 21-29, and 31-34 directly or indirectly depends on claim 20 and is considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

In addition, claims 20-29, 31-34, and 37 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Dmochowski et al., Book of Abstracts, 1998 (item 12, page 4 of the Office Action). This rejection is respectfully traversed.

Claims 20 and 37 recite the methods described above. Dmochowski et al. only disclose methods for rapid injection of electrons and holes to buried active sites in P450 protein. Again, $[Ru(bpy)_3]^{2+}$ can be used as a sensitizer. Dmochowski et al. also describe a method for fast oxidation and reduction of heme of $P450_{cam}$ protein by using Ru(III) and Ru(I) derivatives which are obtained by laser photoexcitation of the sensitizer. There is nothing in Dmochowski et al. disclosing methods for detection of target biomolecules or the modulating agents recited in claims 20 and 37.

Accordingly, Dmochowski et al. fail to disclose every element of claims and, accordingly, is not a proper prior art reference under 35 U.S.C. § 102(a). Consequently, each of claims 20 and 37 is patentably distinguishable over Dmochowski et al. Each of claims 21-29, and 31-34 directly or indirectly depends on claim 20 and is considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

Finally, claims 20-29, 31-34, and 37 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Wilker et al., Book of Abstracts, 1999 (Wilker '99) (item 13, page 5 of the Office Action). This rejection is respectfully traversed.

Claims 20 and 37 recite the methods described above. Wilker '99 only discloses a method for generating enzyme intermediates in buried active sites of the P450 protein, but fails to disclose methods for detection of target biomolecules or the modulating agents recited in claims 20 and 37.

Therefore, Wilker '99 fails to disclose every element of claims and, accordingly, is not a proper prior art reference under 35 U.S.C. § 102(a). Accordingly, each of claims 20 and 37 is patentably distinguishable over Wilker '99. Each of claims 21-29, and 31-34 directly or indirectly depends on claim 20 and is considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

D. Rejection Under 35 U.S.C. § 103 (a)

Claims 30, 35, and 36 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wilker et al., Wilker '98 and Dmochowski et al., or over Wilker '99 and U.S. Patent No. 5,726,041 to Chrespi et al. This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness over a combination of references, the following three basic criteria must be met: (1) there must be some suggestion or motivation to combine the references as proposed by the Examiner; (2) there must be a reasonable expectation of success as a result of such combination; and (3) when all the references are combined, the combination must teach or suggest all of the claim limitations. The Applicants respectfully submits that none of the criteria has been satisfied in this case because the above-mentioned combinations of references fail to teach or suggest every limitation of claims 30, 35, and 36.

Claim 20 recite the methods described above.. As discussed above, none of the Wilker et al., Wilker '98, Wilker '99 or Dmochowski et al. describes a method including "irradiating the complex to cause an emission signal from the sensitizer" in order "to detect the target biomolecule." Therefore, the first combination cited by the Examiner (i.e., Wilker et al., Wilker '98 and Dmochowski et al.) fails to disclose or suggest every limitation of claim 20.

The second combination provided by the Examiner (Wilker '99 and Chrespi et al.) also fails to teach or suggest every limitation of claim 20. Indeed, Wilker '99 discloses a method for generating enzyme intermediates in buried active sites of the P450 protein, but fails to disclose methods for detection of target biomolecules recited in claim 20. Chrespi et al. fail to cure the deficiency of Wilker '99.

Chrespi et al. disclose a detection method which is so different from what is contacting a ligand with a cell that the disclosures of the two references cannot be properly combined. Chrespi et al. require formation of the receptor-ligand complex, wherein a reporter cassette for detecting formation of the receptor-ligand complex must be used. The reporter cassette is essential to the method described in Chrespi et al. because the reporter cassette includes a DNA sequence encoding a cytochrome P450 that is being detected. Chrespi et al. do not disclose method for the detection the target biomolecule that uses no reporter cassette but instead determines the presence of the complex by the signal emitted by the sensitizer, as required by the present claim 20.

Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over the references cited by the Examiner. Claims 30, 35, and 36 depend on claim 20, and are allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456.

Enclosed is check # 573989 in the amount of $60.00 for a One Month Extension of Time. Please charge additional claim fees, or make any credits, to Deposit Account 07-1896.

Respectfully submitted,

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